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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,332	10/08/2003	David L. Shelton	514712000600	8297

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/682,332	SHELTON ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/6/04, 12/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-9, drawn to a method for treating pain comprising administering an anti-nerve growth factor (NGF) antibody and an opioid analgesic, in the reply filed on 23 February 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 10-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 23 February 2006. The Examiner recognizes Applicant's right to pursue additional subject matter in other applications. Therefore, claims 1-11 are pending, and claims 1-9, as they are drawn to a method for treating pain comprising administering an anti-nerve growth factor (NGF) antibody and an opioid analgesic, are under consideration and the subject of this Office Action.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 06 July 2004 and 08 December 2005 have been considered by the examiner.

Specification

4. The disclosure is objected to because of the following informalities:

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "METHODS FOR TREATING PAIN BY ADMINISTERING AN ANTI-NERVE GROWTH FACTOR ANTIBODY AND AN OPIOID ANALGESIC".

6. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See for example, page 35 [0102] and pg 36 [0104]. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ro et al. (Pain. 79:265-274, 1999; cited by Applicants) in view of Zhorov et al. (U.S. Pat. No. 4,389,404).

10. Ro et al. teach administration of anti-NGF antibody for the treatment of pain following constriction injury of the sciatic nerve (See entire document), which is an art-established model of neuropathic pain.

11. The reference of Ro et al. does not teach the co-administration of NGF antibodies and an opioid analgesic, such as morphine.

12. However, the use of the opioid analgesic morphine to treat pain (including post-surgical pain) was known and was routinely used in the art at the time of the invention (See for example Zhorov et al. U.S. Pat. No. 4,389,404; particularly columns 1-2).

13. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to co-administer antibodies to NGF and morphine because the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

14. The person of ordinary skill in the art would have been motivated to make the modification because treatment of pain would alleviate discomfort in the patient, and co-

administration of the antibodies to NGF would permit a lower dosage of morphine, which has well characterized side effects. The expectation of success is high as the treatment of pain with the separate administration of anti-NGF antibodies and opioid analgesics, such as morphine, are documented in the art.

15. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

16. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ro et al. (Pain. 79:265-274, 1999; cited by Applicants) in view of Zhorov et al. (U.S. Pat. No. 4,389,404) as applied to claims 1-3 above, and further in view of Hongo et al. (Hybridoma. 19(3):215-27, 2000; cited by Applicants) and Hoogenboom et al. (WO 93/06213; cited by Applicants).

17. The teachings of Ro et al. and Zhorov et al. are set forth above. Ro et al. and Zhorov et al. do not teach anti-NGF antibodies that bind human NGF, antibodies that bind human NGF with a binding affinity of about 10nM or less than about 10nM. Ro et al. and Zhorov et al. also do not teach human NGF antibodies or humanized NGF antibodies.

18. However, such antibodies as well as methods of making them were known in the art at the time of the invention. Hongo et al. teach humanized antibodies that bind human NGF with a binding affinity of about 10nM or less than 10nM (See pg 217, Table 1). Furthermore, Hoogenboom teach how to make human antibodies (See entire document).

19. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Ro et al. and Zhorov et al. by using the antibodies taught by Hongo et al. and Hoogenboom et al. because humanized and human antibodies offer the

advantage of being more specific for humans and less likely to produce allergic or immune complex sensitivity. (See Hoogenboom et al., pg 1, lines 1-22). The motivation to do so is also provided by Hoogenboom et al. who teach that human or humanized antibodies reduce the likelihood of inappropriate immune responses that interfere with therapy (See pg 1, lines 1-22). The person of ordinary skill in the art would have a reasonable expectation of success because the human or humanized antibodies would likely perform better for the reasons set forth above.

20. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 9-10 of copending Application No. 10/783,730 (US 2004/0253244 A1) in view of Breault et al. (U.S. Pat. No. 5,843,942). Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of 10/783,730 ('730 Application) recite methods for the treatment of pain comprising co-administration of an anti-NGF antibody and a NSAID (non-steroidal anti-inflammatory drug), wherein the antibody binds human NGF, wherein the antibody binds human NGF with a binding affinity of about 10nM or less than about 10nM, and wherein the antibody is human or humanized. Claims 9 and 10 also recite that the pain is post-surgical pain.

23. The claims of the '730 Application do not recite the co-administration of an opioid analgesic with the anti-NGF antibody.

24. However, both the use of opioid analgesics, such as morphine, codeine, and dihydrocodeine, and the use of NSAIDs to treat pain were both known and were routinely used in the art at the time of the invention (See for example Breault et al. (U.S. Pat. No. 5,843,942); particularly column 20, line 27 through column 21, line 9).

25. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the claims of the '730 Application by co-administering an opioid analgesic (morphine), instead of an NSAID, with an anti-NGF antibodies because each of the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

26. The person of ordinary skill in the art would have been motivated to make the modification because treatment of pain would alleviate discomfort in the patient, and co-administration of the antibodies to NGF would permit a lower dosage of morphine, which has well characterized side effects, and patients may require drug changes to overcome a particularly adverse side effect. The expectation of success is high as the treatment of pain with the separate administration of anti-NGF antibodies, NSAIDs, and opioid analgesics, such as morphine, codeine, and dihydrocodeine, are all documented in the art.

27. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

28. Claims 1-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-7 of copending Application No. 10/682,638 in view of Zhorov et al. (U.S. Pat. No. 4,389,404). Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of the 10/682,638 Application ('638 Application) recite methods for the treatment of post-surgical pain comprising administration of an anti-NGF antibody, wherein the antibody binds human NGF, wherein the antibody binds human NGF with a binding affinity of about 10nM or less than about 10nM, and wherein the antibody is human or humanized.

29. The claims of the '638 Application do not recite the co-administration of an opioid analgesic.

30. However, the use of the opioid analgesic morphine to treat pain (including post-surgical pain) was known and was routinely used in the art at the time of the invention (See for example, Zhorov et al., columns 1-2).

31. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the claims of the '638 Application by co-administering morphine with the anti-NGF antibodies because the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

32. The person of ordinary skill in the art would have been motivated to make the modification because treatment of pain would alleviate discomfort in the patient, and co-administration of the antibodies to NGF would permit a lower dosage of morphine, which has well characterized side effects. The expectation of success is high as the treatment of pain with the separate administration of anti-NGF antibodies and opioid analgesics, such as morphine, are documented in the art.

33. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

34. Claims 1-4 and 7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, and 6 of copending Application No. 10/791,162 in view of Zhorov et al. (U.S. Pat. No. 4,389,404). Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of the 10/791,162 Application ('162 Application) recite methods for the treatment of pain comprising administration of an anti-NGF antibody, wherein the antibody binds human NGF and wherein the antibody is humanized.

35. The claims of the '162 Application do not recite the co-administration of an opioid analgesic.

36. However, the use of the opioid analgesic morphine to treat pain (including post-surgical pain) was known and was routinely used in the art at the time of the invention (See for example, Zhorov et al., columns 1-2).

37. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the claims of the '162 Application by co-administering morphine with the anti-NGF antibodies because the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

38. The person of ordinary skill in the art would have been motivated to make the modification because treatment of pain would alleviate discomfort in the patient, and co-administration of the antibodies to NGF would permit a lower dosage of morphine, which has

well characterized side effects. The expectation of success is high as the treatment of pain with the separate administration of anti-NGF antibodies and opioid analgesics, such as morphine, are documented in the art.

39. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

40. Claims 1-4 and 7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20, 22, 36, and 37 of copending Application No. 11/104,248 in view of Zhorov et al. (U.S. Pat. No. 4,389,404). Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of the 11/104,248 Application ('248 Application) recite methods for the treatment of pain comprising administration of an anti-NGF antibody, wherein the antibody binds human NGF and wherein the antibody is humanized.

41. The claims of the '248 Application do not recite the co-administration of an opioid analgesic.

42. However, the use of the opioid analgesic morphine to treat pain (including post-surgical pain) was known and was routinely used in the art at the time of the invention (See for example, Zhorov et al., columns 1-2).

43. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the claims of the '248 Application by co-administering morphine with the anti-NGF antibodies because the molecules are taught individually to be effective for treating pain. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

44. The person of ordinary skill in the art would have been motivated to make the modification because treatment of pain would alleviate discomfort in the patient, and co-administration of the antibodies to NGF would permit a lower dosage of morphine, which has well characterized side effects. The expectation of success is high as the treatment of pain with the separate administration of anti-NGF antibodies and opioid analgesics, such as morphine, are documented in the art.

45. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

46. Claims 1-4 and 6-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 10, and 12-14 of copending Application No. 11/102,201. Although the conflicting claims are not identical, they are not patentably distinct from each other because: The claims of the 11/102,201 Application ('201 Application) recite methods for the treatment of pain comprising administration of an anti-NGF antibody, wherein the antibody binds human NGF, and wherein the antibody is human or humanized. While the claims in the '201 Application do not include the limitation of co-administering an opioid analgesic, it would have been obvious to a person of ordinary skill in the art to co-administer the opioid analgesic as taught in the Instant Application in the treatment methods disclosed in claims 1, 10, and 12-14 of the co-pending '201 Application.

47. The motivation to do so is found in the co-pending '201 Application, which discloses co-administering an opioid analgesic with the anti-NGF antibodies (See pg 2 [0014]). The expectation of success is high as the treatment of pain with both anti-NGF antibodies and opioid analgesics, such as morphine, are documented in the art.

48. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Summary

49. No claim is allowed.

50. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Zahn et al. (2002). Mechanisms for pain caused by incisions. Regional Anesthesia and Pain Medicine. 27(5):514-516.

Brennan et al. (2005). Mechanisms of incisional pain. Anesthesiology Clinics of North America. 23:1-20.

Honore et al. (2000). Murine models of inflammatory, neuropathic and cancer pain each generates a unique set of neurochemical changes in the spinal cord and sensory neurons. Neuroscience. 98(3):585-598.

Honore et al. (2006). Interleukin-1αβ gene-deficient mice show reduced nociceptive sensitivity in modes of inflammatory and neuropathic pain but not post-operative pain.

Gwak et al. (2003). Attenuation of mechanical hyperalgesia following spinal cord injury by administration of antibodies to nerve growth factor in the rat. Neuroscience Letters. 336:117-120.

Zahn et al. (2004). Effect of blockade of nerve growth factor and tumor necrosis factor on pain behaviors after plantar incision. The Journal of Pain. 5(3):157-163.

Brennan, T.J. (1999). Postoperative models of nociception. ILAR Journal. 40(3):129-136.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
May 5, 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER